THE ROLE OF ANTI VEGF INJECTION IN DME WITH VMA

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ESO meeting 2019
Recent Vitreoretinal techniques course

Diabetic macular edema (DME) is the leading cause of visual loss in diabetic patients.

Currently, intravitreal anti-VEGF injections (IVIs) are considered to be the first-line therapy for treatment of DME.

Not sufficient in all cases.

Multifactorial pathogenesis

- One of these factors is ….

the state of vitreoretinal interface

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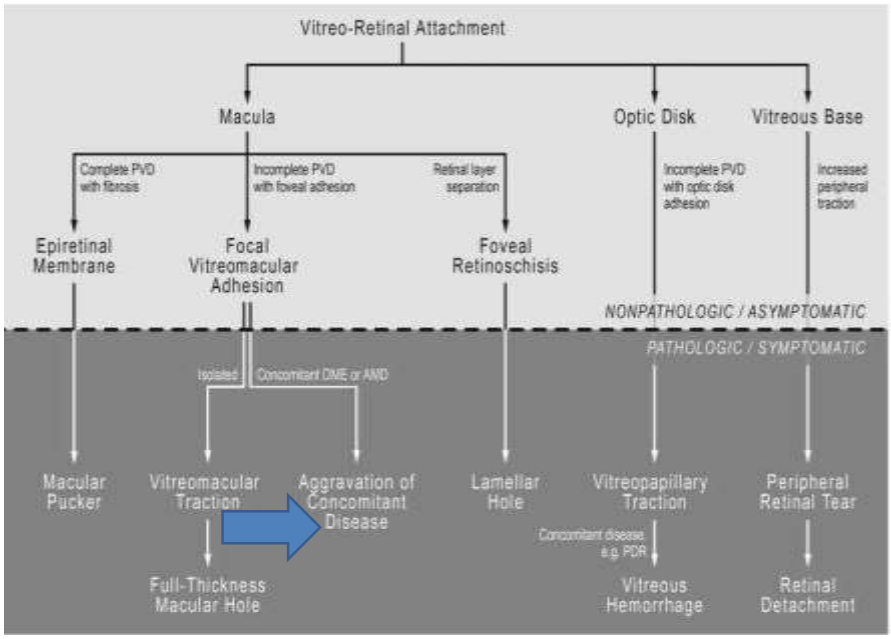
OCT allows evaluation of the vitreoretinal interface (VRI) changes and allows

for a pathogenesis-oriented approach possible for DME therapy.



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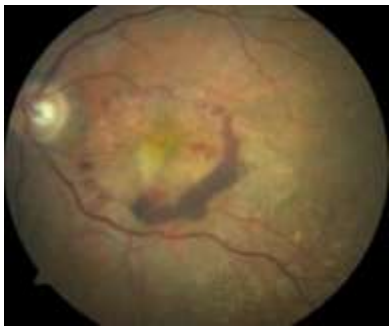
VMA/VMT and DME

Diabetic Macular Edema (DME)

DME with ERM tend to respond **poorly**

DME patients with (+)VMA responded **better** to anti-VEGF than those (-)VMA ***(Sadiq et al)***

VMA/VMT and Neovascular AMD



VMA or VMT can ***decrease the effectiveness*** of anti-VEGF treatment in patients with neovascular AMD

Macular Edema due to Retinal Vein Occlusion

Singh et al. -> found ***no association*** between VRI status and treatment outcomes with anti-VEGF agents for ME secondary to RVO

Which raises the question…

Does anti-VEGF injection induce PVD?

Singh,

Which raises the question…

DOES ANTI-VEGF INJECTION INDUCE PVD?

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PVD and Injections

Could the injection itself regardless of contents induce PVD?

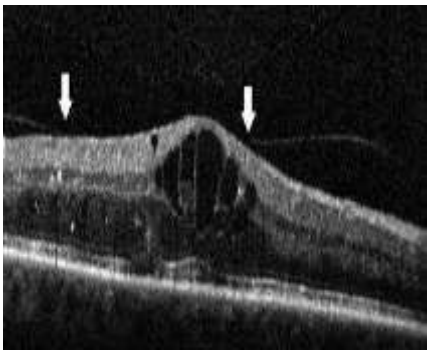
Geck et al. (yes)…DME

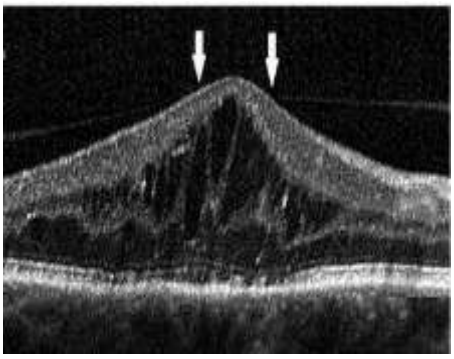
Prospective study of 61 eyes receiving anti-VEGF and had concurrent VMA 15/61 eyes **(24.6%)** developed a PVD

Veloso et al. (no)….AMD

Cohort study of 125 eyes with neovascular AMD and VMA
All received at least 3 monthly anti-VEGF injections (avg 8.3)
7/125 **(5.6%)** eyes developed PVD, all of which had focal VMA

No injection!!!!!





***The International Vitreomacular Traction Study Group Classification*(IVTS)**

Classification and Subclassification

1-VMA:(no change in the contour)

Focal (≤ 1500 µm) or ***broad*** (> 1500 µm)

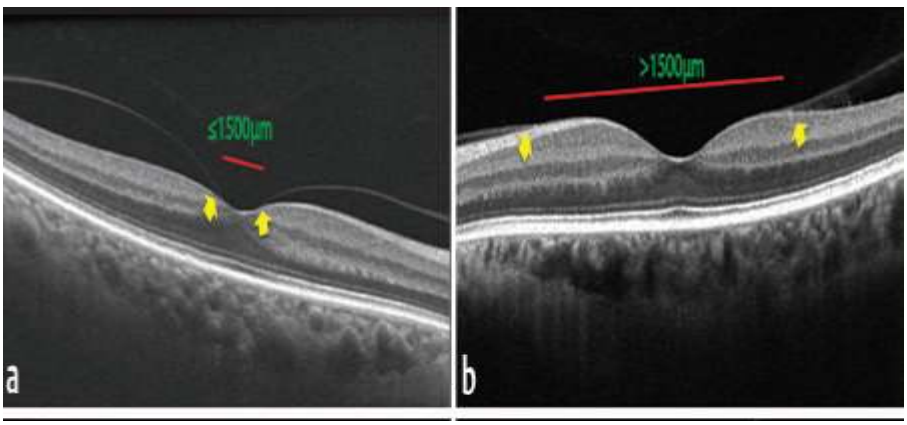
Isolated or concurrent macular disease.

2-VMT: (change in the contour)

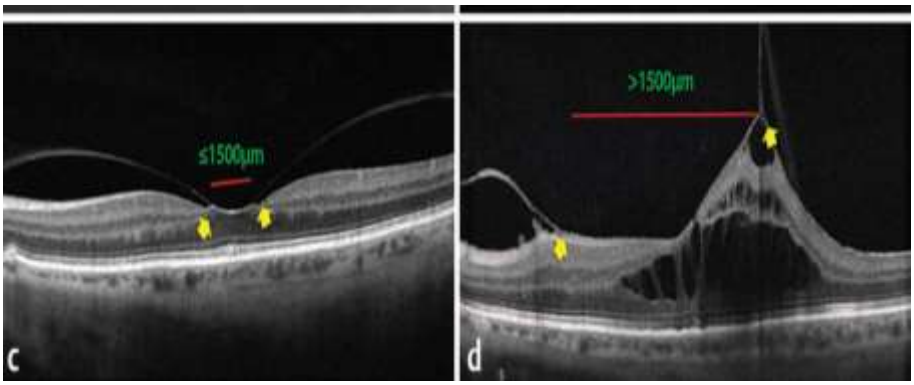
Focal (≤ 1500 µm) or ***broad*** (> 1500 µm)

Isolated or concurrent macular disease

FOCAL VMA BROAD VMA



FOCAL VMT BROAD VMT



VM INTERFACE Abnormalities in DME

Vitreomacular interface disease has been reported to occur in up to **7% to 16%** of eyes with DME.

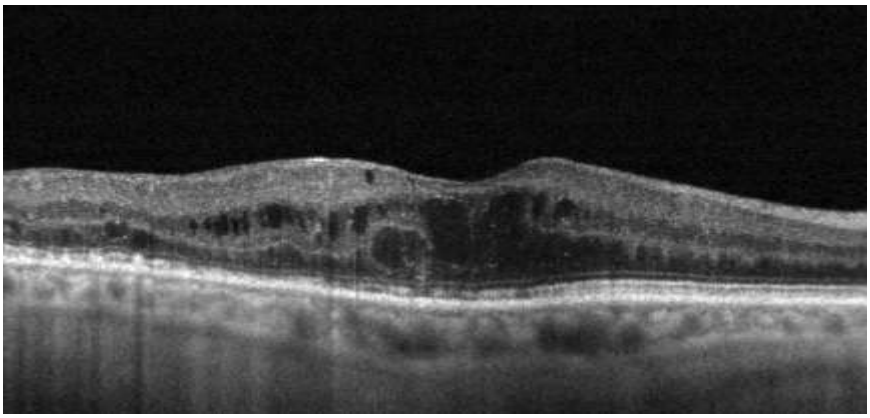
These anomalies include Vitreomacular Traction (VMT), Epiretinal Membrane (ERM), ,Vitreomacular Adhesion (VMA). **(Chang CK,et al; 2012)**

VMA and DME

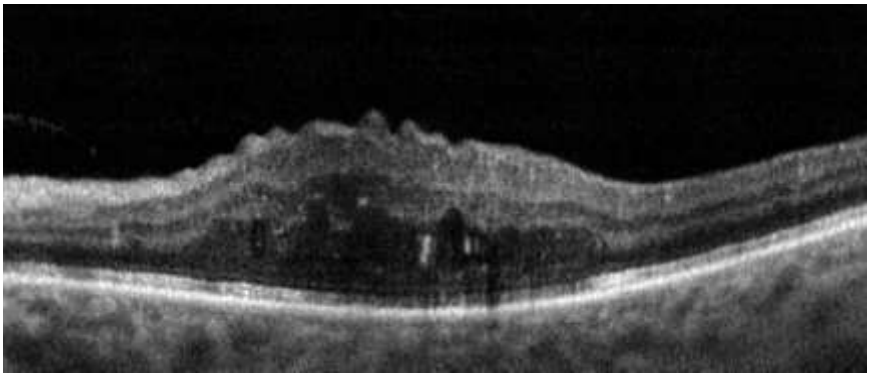
In contrast to DME without VMA:

in these conditions, an increase of retinal thickness is caused not only by upregulation of VEGF and vascular hyperpermeability, but also by anteroposterior or tangential tractions which are followed by ***secondary vascular hyperpermeability*** and retinal thickening.

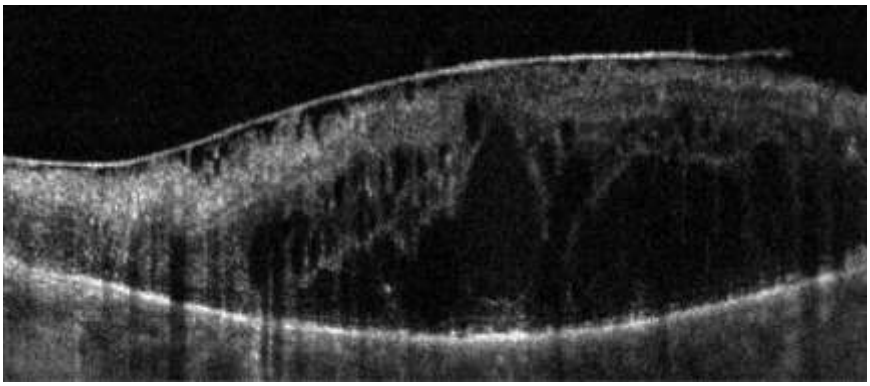
DME with normal VRI



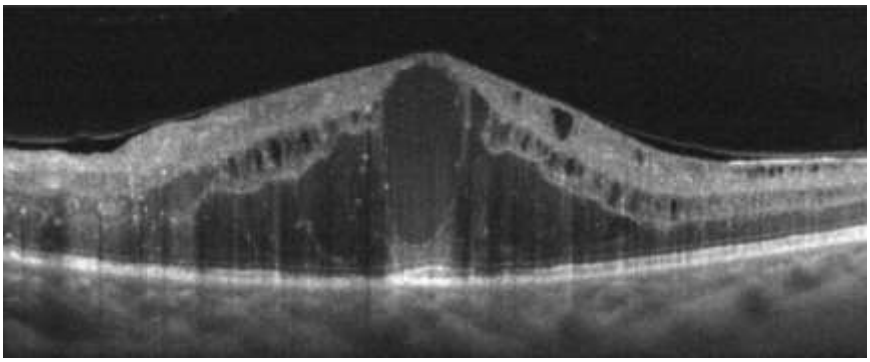
DME with ECCENTRIC ERM



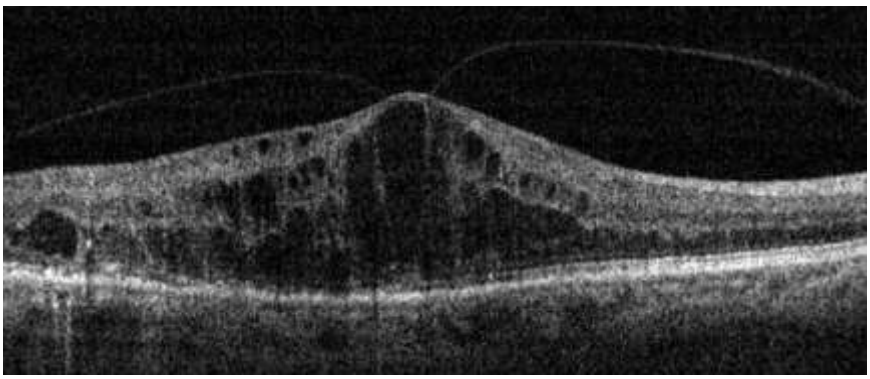
DME with CENTRAL ERM



DME with VMA



DME with VMT



CLINICAL TRIALS

(READ -3)STUDY

***Effect of Vitreomacular* Adhesion on Treatment Outcomes in the Ranibizumab for Edema of the Macula in Diabetes**

(Sadig MA;et al 2016)

READ-3 study

IT is a retrospective cohort study, published in *Ophthalmology in **2016***, evaluated ***26*** patients with DME who had VMA and ***98*** patients with DME who did not have VMA.

Patients were randomized to receive monthly injections of either 0.5 mg of Lucentis for ***6 months***

At the 6-month follow-up,

BCVA increased by a mean of **11.31 ± 6.67** letters in the group **with VMA** and **6.86 ± 7.58** letters in the group **without VMA**. Both increases were significant compared with baseline ($P < .05$), and the difference between the two groups was significant ($P = .007$).

***CONCLUSIONS*:**

DME patients with VMA have a greater potential for improvement in visual outcomes with anti-VEGF.

Therefore, ***the presence of VMA should not preclude patients with DME from receiving treatment. (Sadig MA;et al 2016)***.

The authors attributed the higher visual gains in the group with VMA to an **increased concentration of growth factors in the pre-macular hyaloid secondary to increased enzyme mediated collagen cross-linking in the vitreous.**

"PVD in these eyes may lead to:

1-**Remove this reservoir of growth factor from the vicinity of the retina** and therefore lead to improved outcomes," .

2-**Improved *transvitreal oxygenation*** in these patients after vitreous detachment that may lead to improvement in visual acuity."

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ORIGINAL RESEARCH

Vitreoretinal interface abnormalities in diabetic macular edema and effectiveness of anti-VEGF therapy: an optical coherence tomography study

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Purpose: To study vitreoretinal interface (VRI) abnormalities in diabetic macular edema (DME) and the influence of these on the effectiveness of intravitreal anti-vascular endothelial growth factor (VEGF) therapy.

Methods: VRI status and central retinal thickness (CRT) were evaluated using line and 3D-reference scans obtained using spectral domain-optical coherence tomography RTVue-100 before and 1 month after intravitreal anti-VEGF injection (IVI). VRI status was categorized into five subgroups: normal VRI, retinal surface wrinkling associated with the eccentric epiretinal membrane (ERM), ERM involving the macular center, vitreomacular adhesion (VMA), and vitreomacular traction (VMT).

Results: A total of 105 eyes of 89 patients were included in the study. One month after IVI, the mean change of CRT in normal VRI eyes and eyes with VRI abnormalities was −128.0±144.7 µm and −53.0±96.4 µm ($p<0.05$), respectively. The mean change of CRT 1 month after IVI in each subgroup with VRI abnormalities, apart from the subgroup with retinal wrinkling associated with eccentric ERM, was statistically significantly lower compared to the eyes with normal VRI ($p<0.05$).

Conclusion: VRI abnormalities significantly reduce the effectiveness of intravitreal anti-VEGF therapy in eyes with DME. Eyes with noticeable changes of VRI, including ERM involving the macular center, VMA, and VMT have a poorer response to anti-VEGF therapy compared to eyes with normal VRI or eccentric ERM.

Keywords: diabetic macular edema, anti-VEGF, optical coherence tomography, epiretinal membrane, vitreomacular adhesion, vitreomacular traction

LIMITATION: only **one month** follow up

VMA associated with poor outcomes in anti-VEGF-treated patients

Cheryl Guttman Krader,Jul 20, 2017

The study included 195 eyes treated since 2012

The presence of vitreomacular adhesion (VMA) is associated with poorer, short-term anatomic, and functional outcomes in eyes with diabetic macular edema (DME) receiving anti-VEGF therapy **(Márcio B. Nehemy)**

Mean BCVA :

the mean BCVA at ***1 month*** was better in the VMA-negative group than in the VMA-positive group.

Central retinal thickness :

the magnitude of improvement was greater in VMA-negative eyes.

In the eye that presented VMA release after six injections had a better anatomic and visual outcome

LIMITATION: only **one month** follow up

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Official Publication of
Egyptian Vitreoretinal Society (EGVRS)

Medknow

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Original Article

Benefits of Anti-Vascular Endothelial Growth Factor Therapy for Diabetic Macular Edema with and without Vitreomacular Adhesions

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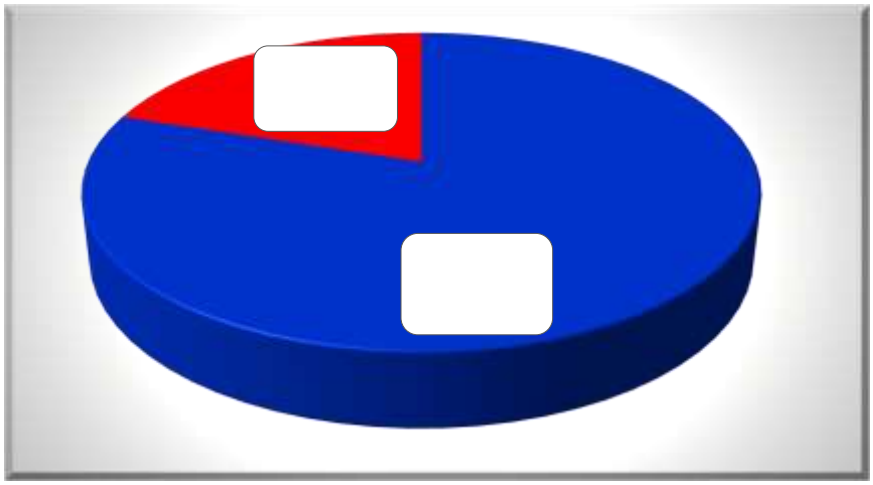
Abstract

Purpose: We aimed to evaluate the effect of vitreomacular adhesion (VMA) in visual and anatomic outcomes in patients with diabetic macular edema (DME) after intravitreal injection of ranibizumab (Lucentis®). **Patients and Methods:** This was a prospective cohort study that included thirty eyes of DME patients, divided into two groups according to their spectral-domain-optical coherence tomography image analysis at the baseline visit to identify the presence (VMA+) or absence (VMA−) of VMA. Patients with any degree of vitreomacular traction were not included in this study. VMA was classified by the size of adhesion into either focal (<1500 mm) or broad (>1500 mm). All patients received monthly 0.5 mg of intravitreal ranibizumab injection for 6 months. Patients were observed monthly for a 6-month period and their best-corrected visual acuity (BCVA) and central macular thickness (CMT) were recorded. The incidence of posterior vitreous detachment (PVD) was observed. **Results:** Compared with baseline, there was a significant decrease in CMT after 6 months by 151.46 ± 121.47 and 139.33 ± 144.23 μm in VMA+ and VMA− groups, respectively ($P = 0.681$). The mean average improvement in BCVA was 10.21 ± 6.33 and 6.68 ± 6.35 letters in the VMA+ and VMA− groups, respectively. The difference between the two groups was statistically significant ($P = 0.007$). At 6 months, among the 15 eyes of VMA+ at baseline, 4 eyes demonstrated PVD and 11 eyes showed no change in VMA status. **Conclusion:** Patients having DME with VMA may achieve higher visual gain with anti-vascular endothelial growth factor therapy. Presence of VMA should not preclude patients with DME from receiving anti-vascular endothelial growth factor therapy.

Keywords: Anti-vascular endothelial growth factor, diabetic macular edema, vitreomacular adhesion

Vitreomacular adhesion status change after 6 month in VMA+ group.



Focal versus broad VMA changes after 6 month.

	VMA+ (n=15)	
	Focal VMA	Broad VMA
Mean BCVA change from baseline To month 6 (letters)		
Mean±SD	11.40±2.85	12.35±6.26
P value	0.82	0.62
Mean CMT change from baseline To month 6 (µm)		
Mean ±SD	300.000± 132.82	154.89± 112.45
P value	0.02	0.03

Of the four patients in which PVD developed:

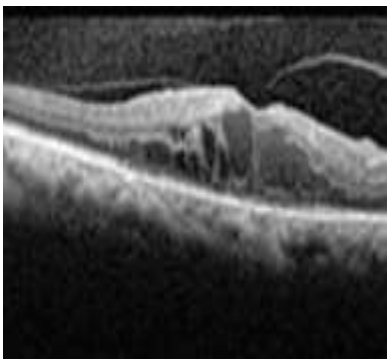
2 patients demonstrated PVD after the first injection

one patient demonstrated PVD

after five injections.

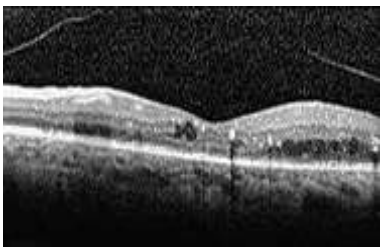
and one patient demonstrated PVD after six injections.

Baseline



CST: 449 µm
(20/50)

M6



CST: 269 µm
(20/30)

Sum of the studies

-Studies in in which the presence of VMA has better outcome had a long follow up

(6 months)

While, studies in which the presence of VMA has poor outcome had a short follow up

(one month)

Home message

So, we recommend to extend the number of injection in patient with DME with VMA to

6 initial injections instead of 3 or 4 injections

for a better outcome and higher incidence of post injection PVD

الحمد لله رب العالمين